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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/171,885 10/28/98 CUBICCIOTTI

R BDA-0038

HM12/0605

EXAMINER

JANE MASSEY LICATA  
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WARE, T

ART UNIT	PAPER NUMBER
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1615

*21*

DATE MAILED:

06/05/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/171,885	CUBICCIOTTI, ROGER S.
	Examiner Todd D Ware	Art Unit 1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 03 May 2001.

2a) This action is FINAL.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 13-29 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 13-29 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

15) Notice of References Cited (PTO-892)      18) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.

16) Notice of Draftsperson's Patent Drawing Review (PTO-948)      19) Notice of Informal Patent Application (PTO-152)

17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.      20) Other: \_\_\_\_\_

## DETAILED ACTION

Receipt of request for extension of time and preliminary amendment filed 5-3-01 is acknowledged. Claims 13, 14, 16, 18, 20, 22, 24, 26, and 28 have been amended as requested. Claims 13-29 are pending.

The request filed on 5-3-01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/171,885 is acceptable and a CPA has been established. An action on the CPA follows.

**Please note.** In an earnest effort to advance the prosecution of this application, it is suggested that an interview between the inventor, the inventor's attorney, the examiner of record and a primary examiner may be in order either by teleconference or "in person" at the USPTO. The applicants' attorney is therefore invited to contact the examiner of record regarding such an interview.

### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
2. Claims 14-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Recitation of "a drug bound to a synthetic receptor selected to bind said drug by a method selected from..." is unclear. As written, this may be understood to claim that combinatorial selection, monoclonal antibody selection and antibody engineering are

methods by which the drug binds to a synthetic receptor while it appears that applicants are attempting to claim that the synthetic receptor is identified or is selected by either combinatorial selection, monoclonal antibody selection or antibody engineering.

Correction is requested.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 13-29 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Morgan, Jr. et al (5,106,951; hereafter '951).

'951 discloses drug/carrier complexes and a method of administering a drug via a drug/carrier complex where a drug binds to a polymeric carrier to form a prodrug complex that is capable of allowing drug dissociation from the polymeric carrier such that the drug retains its ability to bind to a site on or within a target cell. The "antibody csDBM complex" of '951 is considered the synthetic receptor. Since '951 states that the drug's ability to bind to a higher affinity site on or within the target cell is retained (abstract; C4, L43-C5, L25; C8, L30-40; C18, L43-48), the conjugate of '951 binds preferentially to the "pathophysiologic receptor" (the higher affinity site on or within the target cell). '951 also discloses that the drug-conjugate is not exposed to derivatization conditions that might compromise the potency of the drug (i.e. the drug is immobilized

and is protected from metabolism which would increase its half-life over administration of the drug alone) (C4, L43-50). '951 further discloses that targeting proteins may be attached to the conjugate.(C7, L10-19, 30-37). The carriers of '951 may also bind more than one drug (C10, L62-66). Column 5, lines 11-17 discloses the "csDBM is specifically designed to fit the drug molecule and undergo multiple non-covalent interactions with a drug." Thus, the limitations reciting that the drug is specifically bound to the synthetic receptor via noncovalent interactions between the selected drug and the synthetic receptor are met by '951. The methods used to identify the conjugate are not considered patentably distinct as they are intended use limitations. Furthermore, the antibodies of '951 would be readily identifiable by the instant methods.

***Response to Arguments***

5. Applicant's arguments filed 5-3-01 have been fully considered but they are not persuasive. Applicant argues that '951 discloses that the csDBM is covalently bound to the antibody or carrier and noncovalently complexed to a drug molecule and that this is different from the instant claims since the instant claims recite that the drug is noncovalently complexed to the synthetic receptor. It is not understood how '951 and the instant claims are different. '951 discloses noncovalent binding of the drug to the csDBM-antibody complex and the instant claims require noncovalent binding of the drug to the synthetic receptor. The csDBM-antibody complex of '951 meets the requirement of a synthetic receptor. Further clarification is requested.

Applicant also argues that the instant claims require noncovalent binding between the drug and the synthetic receptor and that '951 discloses noncovalent

binding between the drug and the csDBM-antibody complex. Again this argument is not understood as the csDBM-antibody complex of '951 meets the requirement of a synthetic receptor. Further clarification is requested.

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 13-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan, Jr. et al. (5,106,951; hereafter '951).

'951 teaches drug/carrier complexes and a method of administering a drug via a drug/carrier complex where a drug binds to a polymeric carrier to form a prodrug complex that is capable of allowing drug dissociation from the polymeric carrier such that the drug retains its ability to bind to a site on or within a target cell. The "antibody csDBM complex" of '951 is considered the synthetic receptor. Since '951 states that the drug's ability to bind to a higher affinity site on or within the target cell is retained (abstract; C4, L43-C5, L25; C8, L30-40; C18, L43-48), the conjugate of '951 binds preferentially to the "pathophysiologic receptor" (the higher affinity site on or within the target cell). '951 also discloses that the drug-conjugate is not exposed to derivatization conditions that might compromise the potency of the drug (i.e. the drug is immobilized and is protected from metabolism which would increase its half-life over administration

of the drug alone) (C4, L43-50). '951 further discloses that targeting proteins may be attached to the conjugate.(C7, L10-19, 30-37). The carriers of '951 may also bind more than one drug molecule (C10, L62-66). Column 5, lines 11-17 discloses the "csDBM is specifically designed to fit the drug molecule and undergo multiple non-covalent interactions with a drug." Thus, the limitations reciting that the drug is specifically bound to the synthetic receptor via noncovalent interactions between the selected drug and the synthetic receptor are met by '951. The methods used to identify the conjugate are not considered patentably distinct as they are intended use limitations. Furthermore, the antibodies of '951 would be readily identifiable by the instant methods.

'951 does not specifically state that the carriers of '951 may bind multiple drugs wherein the drugs are different. '951 does state that the carriers have multiple drug-binding regions capable of binding multiple drug molecules. Therefore, it would be obvious to one skilled in art at the time of the invention to design the conjugates of '951 wherein the domains would be different would be capable of binding more than one drug where the drugs are different with the expectation that administering more than one drug to treat a condition would result in an additive treatment effect with the motivation of protecting the drug against metabolism or other factors that might reduce potency.

#### ***Response to Arguments***

8. Applicant's arguments filed 5-3-01 have been fully considered but they are not persuasive. Applicant argues that '951 discloses that the csDBM is covalently bound to the antibody or carrier and noncovalently complexed to a drug molecule and that this is

different from the instant claims since the instant claims recite that the drug is noncovalently complexed to the synthetic receptor. It is not understood how '951 and the instant claims are different. '951 discloses noncovalent binding of the drug to the csDBM-antibody complex and the instant claims require noncovalent binding of the drug to the synthetic receptor. The csDBM-antibody complex of '951 meets the requirement of a synthetic receptor. Further clarification is requested.

Applicant also argues that the instant claims require noncovalent binding between the drug and the synthetic receptor and that '951 discloses noncovalent binding between the drug and the csDBM-antibody complex. Again this argument is not understood as the csDBM-antibody complex of '951 meets the requirement of a synthetic receptor. Further clarification is requested.

### ***Conclusion***

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Todd D Ware whose telephone number is (703) 305-1700. The examiner can normally be reached on 8:30 am - 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703)308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) for regular communications and (703) for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

tw  
June 1, 2001

  
THURMAN K. PAGE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600